NOV 8 2000

NDA 8-085/S-046
NDA 11-719/S-096

Lederle Parenterals, Inc.
Attention: Nanette B. Hoiston
P.O. Box 8299
Philadelphia, Pennsylvania 19101

Dear Ms. Hoiston:

Please refer to your October 15, 1997 supplemental new drug applications, NDA 8-085/5-046 and NDA 1 l-917/S-096, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Methotrexate Sodium Tablets, Methotrexate Sodium for Injection and Methotrexate Sodium Injection.

We acknowledge receipt of your July 31 and October 17, 2000 communications.

The equivalent submissions provide for revisions in the text of the physician's package insert for additional information under CLINICAL PHARMACOLOGY, Pharmacokinetics, INDICATIONS AND USAGE, Pediatric Use, ADVERSE REACTIONS, and DOSAGE AND ADMINISTRATION sections regarding the use of methotrexate in the pediatric population.

We have completed our review of these applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the agreed upon labeling text. Accordingly, the applications are approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted labeling (text for package insert/attachment A) submitted October 15, 1997, as modified by your July 31 and October 17, 2000 agreements, and must be formatted in accordance with the requirements of2l CFR 201.66.

Please submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed to each application. Please mount individually ten of the copies on heavy-weight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled Providing Regulatory Submissions in Electronic Format – NDAs (January 1999). For administrative purposes, these submissions should be designated "FPL for approved supplement NDA 8-805/S-046" and "FPL for approved supplement 11-719/S-096". Approval of these submissions by FDA is not required before the labeling is used.

Please also respond to the following comments which were provided in our May 20, 1997 approval letter for NDA 8-805/S-045 and NDA 11-719/S-095.

1. We recommend that in the How Supplied section of the proposed labeling in the package insert, the storage statement

   "Store between 15-250C(59F-77F)"

   should be changed to

   "Store at 25C(77F); excursions permitted to 15-30C(59-86F) [see USP Controlled Room Temperature]"

2. The color of each of the caps should be listed in the How Supplied section of the package insert for Methotrexate Sodium for Injection, Methotrexate LPF Sodium, and Methotrexate Sodium Injection.

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Paul Zimmerman, Project Manager, at (301) 594-5775.

Sincerely,

Richard Pazdur, M.D.
Director
Division of Oncologic Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Final printed labeling not available through OGD